

# Naval Medical Center Portsmouth (NMCP) COVID-19 Literature Report #99: Friday, 05 August 2022

**ANNOUNCEMENT:** The NMCP COVID-19 Literature Report has been produced since March 2020. These reports have taken significant time and effort to produce, often at the cost of other demands. **These reports will end with the next one, #100, on 19 August 2022.** I hope they have been of value. Archived reports will be available [online](#) and through the [Medical Heritage Library](#) and [BUMED's Office of Medical History collection](#) at archive.org.

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**Purpose:** These reports, published every other week on Fridays, are curated collections of current research, special reports, and news regarding the COVID-19 pandemic that may be of interest to medical providers, leadership, and decision makers. All reports are available online at <https://nmcp.libguides.com/covidreport>.

**Disclaimer:** I am not a medical professional. This document is current as of the date noted above. While I make every effort to find and summarize available data, I cannot cover everything in the literature on COVID-19. Due to the rapid evolution of the literature, I will not update past reports when new information arises; for retracted papers specific to COVID-19, see the [list of retracted papers from Retraction Watch](#).

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## The Big Picture

### *News in Brief*

"Covid has settled into a persistent pattern — and remains damaging. It may not change anytime soon" ([STAT](#)).

The Origins of Covid-19 are more complicated than once thought" ([Wired](#)).

"Pentagon biological defense programs at 'pivot point'" ([Nat Def Mag](#)).

### *Journal Articles*

Clin Infect Dis: [Measuring work-related risk of COVID-19: comparison of COVID-19 incidence by occupation and industry – Wisconsin, September 2020-May 2021](#) (04 August 2022)

"Background: Work-related exposures play an important role in SARS-CoV-2 transmission, yet few studies have measured the risk of COVID-19 across occupations and industries.

Methods: During September 2020 - May 2021, the Wisconsin Department of Health Services collected occupation and industry data as part of routine COVID-19 case investigations. Adults aged 18-64 years with confirmed or probable COVID-19 in Wisconsin were assigned standardized occupation and industry codes. Cumulative incidence rates were weighted for non-response and calculated using full-time equivalent (FTE) workforce denominators from the 2020 American Community Survey.

Results: An estimated 11.6% of workers (347,013 of 2.98 million) in Wisconsin, ages 18-64 years, had COVID-19 from September 2020 to May 2021. The highest incidence by occupation (per 100 full-time equivalents) occurred among personal care and services workers (22.4), healthcare practitioners and support staff (20.7), and protective services workers (20.7). High risk sub-groups included nursing assistants and personal care aides (28.8), childcare workers (25.8), food and beverage service workers (25.3), personal appearance workers (24.4), and law enforcement workers (24.1). By industry, incidence was highest in healthcare (18.6); the highest risk sub-sectors were nursing care facilities (30.5) and warehousing (28.5).

Conclusions: This analysis represents one of the most complete examinations to date of COVID-19 incidence by occupation and industry. Our approach demonstrates the value of standardized occupational data collection by public health, and may be a model for improved occupational surveillance elsewhere. Workers at higher risk of SARS-CoV-2 exposure may benefit from targeted workplace COVID-19 vaccination and mitigation efforts."

## COVID-19 Vaccines

### *News in Brief*

"How many lives could a fall COVID-19 booster campaign save in the United States?" ([CF](#))

"Second coronavirus booster shots for people under 50 on hold amid drive to speed up new vaccine" ([WP](#)).

### *Journal Articles*

MMWR: [Interim Recommendation of the Advisory Committee on Immunization Practices for Use of the Novavax COVID-19 Vaccine in Persons Aged ≥18 years — United States, July 2022](#) (05 August 2022)

"What is already known about this topic? On July 13, 2022, the Food and Drug Administration issued Emergency Use Authorization for the NVX-CoV2373 (Novavax) COVID-19 vaccine.

What is added by this report? On July 19, 2022, the Advisory Committee on Immunization Practices made an interim recommendation for use of the Novavax vaccine in persons aged ≥18 years as a primary 2-dose series vaccination for the prevention of COVID-19.

What are the implications for public health practice? The adjuvanted, protein subunit–based Novavax COVID-19 vaccine provides an additional option for unvaccinated adults, increasing flexibility for the public and for vaccine providers. Vaccination is important for protection against COVID-19."

MMWR: [Safety Monitoring of COVID-19 mRNA Vaccine Second Booster Doses Among Adults Aged ≥50 Years — United States, March 29, 2022–July 10, 2022](#) (29 July 2022)

"What is already known about this topic? During March 29–July 10, 2022, approximately 16.8 million persons in the United States aged ≥50 years received a fourth dose of a COVID-19 vaccine.

What is added by this report? Among persons aged ≥50 years who reported homologous mRNA COVID-19 vaccination, injection site and systemic reactions were less frequent after a second booster dose than after the first booster dose. Ninety-five percent of 8,515 events reported to the Vaccine Adverse Event Reporting System were nonserious.

What are the implications for public health practice? Health care providers and patients should be aware that local and systemic reactions are expected after a second mRNA COVID-19 booster dose. Serious adverse events are uncommon."

JAMA Netw Open: [Effectiveness Associated With Vaccination After COVID-19 Recovery in Preventing Reinfection](#) (27 July 2022)

"Question: How effective is vaccination against COVID-19 after recovery from prior SARS-CoV-2 infection?

Findings: In this cohort study of more than 95 000 Rhode Island residents from March 2020 to December 2021, including residents and employees of long-term congregate care (LTCC) facilities, completion of the primary vaccination series after recovery from COVID-19 was associated with 49% protection from reinfection among LTCC residents, 47% protection among LTCC employees, and 62% protection in the general population during periods when wild type, Alpha, and Delta strains of SARS-CoV-2 were predominant.

Meaning: These findings suggest that among people who have recovered from COVID-19, subsequent completion of the primary vaccination series reduced the risk of reinfection by approximately half."

## Transmission, Exposure, and Surveillance

### *News in Brief*

"America is running out of 'COVID virgins'" ([Atlantic](#)).

"Could genetics be the key to never getting the coronavirus?" ([Atlantic](#))

"How long is COVID infectious? What scientists know so far — Those with SARS-CoV-2 are often advised to isolate for only a few days. But evidence is mounting that some people can continue to pass on the virus for much longer" ([Nature](#)).

"When you have covid, here's how you know you are no longer contagious" ([WP](#)).

### *Journal Articles*

JAMA Netw Open: [Duration of Symptoms and Association With Positive Home Rapid Antigen Test Results After Infection With SARS-CoV-2](#) (03 August 2022)

"In this cohort study of individuals newly diagnosed with COVID-19, 75% continued to have positive RAT results, while 35% had culturable virus on day 6. Everyone with a negative day-6 RAT result had a negative viral culture. However, only 50% of those with a positive RAT result had culturable virus. Acknowledging the caveats of a small cohort of mostly young, vaccinated, nonhospitalized individuals with a presumed Omicron variant and potential

variation in self-sampling techniques and lab-based culture methods, these data suggest that a negative RAT result in individuals with residual symptoms could provide reassurance about ending isolation."

J Infect Dis: [Sensitivity of RT-PCR tests for SARS-CoV-2 through time](#) (25 July 2022)

"Reverse transcriptase polymerase chain reaction (RT-PCR) tests are the gold standard for detecting recent infection with SARS-CoV-2. RT-PCR sensitivity varies over the course of an individual's infection, related to changes in viral load. Differences in testing methods, and individual-level variables such as age, may also affect sensitivity. Using data from New Zealand, we estimate the time-varying sensitivity of SARS-CoV-2 RT-PCR under varying temporal, biological and demographic factors. Sensitivity peaks 4-5 days post-infection at 92.7% [91.4%, 94.0%] and remains over 88% between 5 and 14 days post-infection. After the peak, sensitivity declined more rapidly in vaccinated cases compared to unvaccinated, females compared to males, those aged under 40 compared to over 40 s, and Pacific peoples compared to other ethnicities. RT-PCR remains a sensitive technique and has been an effective tool in New Zealand's border and post-border measures to control COVID-19. Our results inform model parameters and decisions concerning routine testing frequency."

## Treatments and Management

### *News in Brief*

"A randomized phase IIa trial of an investigational long COVID treatment failed to meet its primary endpoint, said Axcella Therapeutics, but the company highlighted patient improvements in mental and physical fatigue versus the placebo group" ([Medpage](#); see also: [Axcella press release](#)).

### *Journal Articles*

J Infect Dis: [Hyperimmune globulin for severely immunocompromised patients hospitalized with COVID-19: a randomized, controlled trial](#) (04 August 2022)

"The aim of this randomized, controlled trial is to determine whether anti-SARS-CoV-2 hyperimmune globulin protects against severe COVID-19 in severely immunocompromised, hospitalized, COVID-19 patients. Patients were randomly assigned to receive anti-SARS-CoV-2 hyperimmune globulin (COVIG) or intravenous immunoglobulin without SARS-CoV-2 antibodies. Severe COVID-19 was observed in two out of ten (20%) patients treated with COVIG compared to seven out of eight (88%) in the IVIG control group ( $p = 0.015$ , Fisher's

exact test). COVIG may be a valuable treatment in severely immunocompromised, hospitalized, COVID-19 patients and should be considered when no monoclonal antibody therapies are available."

JAMA: [Development of Resistance-Associated Mutations After Sotrovimab Administration in High-risk Individuals Infected With the SARS-CoV-2 Omicron Variant](#) (01 August 2022)

"This study found rapid development of sotrovimab resistance–associated mutations at positions S:E340 and S:P337 in a large proportion of high-risk patients infected with the Omicron variant after treatment with sotrovimab, which was associated with a delay in viral clearance. These results are in line with a report describing the occurrence of resistance mutations 6 to 13 days after treatment with sotrovimab in patients infected with the Delta variant."

PLoS One: [Prevalence of bacterial coinfection and patterns of antibiotics prescribing in patients with COVID-19: A systematic review and meta-analysis](#) (01 August 2022)

"Background: Evidence around prevalence of bacterial coinfection and pattern of antibiotic use in COVID-19 is controversial although high prevalence rates of bacterial coinfection have been reported in previous similar global viral respiratory pandemics. Early data on the prevalence of antibiotic prescribing in COVID-19 indicates conflicting low and high prevalence of antibiotic prescribing which challenges antimicrobial stewardship programmes and increases risk of antimicrobial resistance (AMR).

Aim: To determine current prevalence of bacterial coinfection and antibiotic prescribing in COVID-19 patients.

Data source: OVID MEDLINE, OVID EMBASE, Cochrane and MedRxiv between January 2020 and June 2021.

Study eligibility: English language studies of laboratory-confirmed COVID-19 patients which reported (a) prevalence of bacterial coinfection and/or (b) prevalence of antibiotic prescribing with no restrictions to study designs or healthcare setting.

Participants: Adults (aged  $\geq 18$  years) with RT-PCR confirmed diagnosis of COVID-19, regardless of study setting.

Methods: Systematic review and meta-analysis. Proportion (prevalence) data was pooled using random effects meta-analysis approach; and stratified based on region and study design.

Results: A total of 1058 studies were screened, of which 22, hospital-based studies were eligible, compromising 76,176 of COVID-19 patients. Pooled estimates for the prevalence of bacterial co-infection and antibiotic use were 5.62% (95% CI 2.26-10.31) and 61.77% (CI

50.95-70.90), respectively. Sub-group analysis by region demonstrated that bacterial co-infection was more prevalent in North American studies (7.89%, 95% CI 3.30-14.18).

Conclusion: Prevalence of bacterial coinfection in COVID-19 is low, yet prevalence of antibiotic prescribing is high, indicating the need for targeted COVID-19 antimicrobial stewardship initiatives to reduce the global threat of AMR."

Clin Infect Dis: [Tenofovir Disoproxil Fumarate/Emtricitabine and Baricitinib for Patients at High Risk of Severe COVID-19: The PANCOVID Randomized Clinical Trial](#) (30 July 2022)

"Background: This study was designed to evaluate if patients with high risk for severe COVID-19 would benefit from treatment with TDF/FTC followed by baricitinib in case of hypoxemia and systemic inflammation.

Methods: PANCOVID is an open-label, double-randomized, phase 3 pragmatic clinical trial including adults with symptomatic COVID-19 with  $\geq 2$  comorbidities or older than 60 years conducted between 10 October 2020 and 23 September 2021. In the first randomization patients received TDF/FTC or not TDF/FTC. In the second randomization patients with room-air O<sub>2</sub> saturation  $<95\%$  and at least one increased inflammatory biomarker received baricitinib plus dexamethasone or dexamethasone alone. The primary endpoint was 28-day mortality. Main secondary endpoint was 28-day disease progression or critical care unit admission or mortality. The trial was stopped before reaching planned sample size due to the decrease in the number of cases and a mortality rate substantially lower than expected EudraCT registration number: 2020-001156-18.

Results: Of the 355 included participants 97% were hospitalized at baseline. Overall, 28-day mortality was 3.1%. The 28-day mortality relative risk (RR) for participants treated with TDF/FTC was 1.76 (95% CI 0.52-5.91;  $p = 0.379$ ); it was 0.42 (95% CI 0.11-1.59;  $p = 0.201$ ) for those treated with baricitinib. The 28-day RR for the main secondary combined endpoint for participants treated with TDF/FTC was 0.95 (95% CI 0.66-1.40;  $p = 0.774$ ); it was 0.90 (95% CI 0.61-1.33;  $p = 0.687$ ) for those treated with baricitinib.

Conclusions: Our results do not suggest a beneficial effect of TDF/FTC; nevertheless, they are compatible with the beneficial effect of baricitinib already established by other clinical trials."

J Infect Dis: [Casirivimab and Imdevimab for the Treatment of Hospitalized Patients With COVID-19](#) (27 July 2022)

"Background: The open-label RECOVERY study reported improved survival in hospitalized, SARS-CoV-2 seronegative patients treated with casirivimab and imdevimab (CAS + IMD).

Methods: In this phase I/II/III, double-blind, placebo-controlled trial conducted prior to widespread circulation of Delta and Omicron, hospitalized COVID-19 patients were



randomized (1:1:1) to 2.4 g or 8.0 g CAS + IMD or placebo, and characterized at baseline for viral load and SARS-CoV-2 serostatus.

Results: 1336 patients on low-flow or no supplemental (low-flow/no) oxygen were treated. The primary endpoint was met: in seronegative patients, the least-squares mean difference (CAS + IMD versus placebo) for time-weighted average change from baseline in viral load through day 7 was -0.28 log<sub>10</sub> copies/mL (95% CI, -0.51 to -0.05; P = .0172). The primary clinical analysis of death or mechanical ventilation (death/MV) from day 6-29 in patients with high viral load had a strong positive trend but did not reach significance. CAS + IMD numerically reduced all-cause mortality in seronegative patients through day 29 (relative risk reduction, 55.6%; 95% CI, 24.2-74.0). No safety concerns were noted.

Conclusions: In hospitalized COVID-19 patients on low-flow/no oxygen, CAS + IMD reduced viral load and likely improves clinical outcomes in the overall population, with the benefit driven by seronegative patients, and no harm observed in seropositive patients."

CMAJ: [Antiviral drug treatment for nonsevere COVID-19: a systematic review and network meta-analysis](#) (25 July 2022)

"Background: Randomized trial evidence suggests that some antiviral drugs are effective in patients with COVID-19. However, the comparative effectiveness of antiviral drugs in nonsevere COVID-19 is unclear.

Methods: We searched the Epistemonikos COVID-19 L-OVE (Living Overview of Evidence) database for randomized trials comparing antiviral treatments, standard care or placebo in adult patients with nonsevere COVID-19 up to Apr. 25, 2022. Reviewers extracted data and assessed risk of bias. We performed a frequentist network meta-analysis and assessed the certainty of evidence using the Grading of Recommendations, Assessment, Development and Evaluation (GRADE) approach.

Results: We identified 41 trials, which included 18 568 patients. Compared with standard care or placebo, molnupiravir and nirmatrelvir-ritonavir each reduced risk of death with moderate certainty (10.9 fewer deaths per 1000, 95% confidence interval [CI] 12.6 to 4.5 fewer for molnupiravir; 11.7 fewer deaths per 1000, 95% CI 13.1 fewer to 2.6 more). Compared with molnupiravir, nirmatrelvir-ritonavir probably reduced risk of hospital admission (27.8 fewer admissions per 1000, 95% CI 32.8 to 18.3 fewer; moderate certainty). Remdesivir probably has no effect on risk of death, but may reduce hospital admissions (39.1 fewer admissions per 1000, 95% CI 48.7 to 13.7 fewer; low certainty).

Interpretation: Molnupiravir and nirmatrelvir-ritonavir probably reduce risk of hospital admissions and death among patients with nonsevere COVID-19. Nirmatrelvir-ritonavir is probably more effective than molnupiravir for reducing risk of hospital admissions. Most trials were conducted with unvaccinated patients, before the emergence of the Omicron



variant; the effectiveness of these drugs must thus be tested among vaccinated patients and against newer variants."

### *Disparities*

JAMA Netw Open: [Assessment of Exposure to Environmental Toxins and Racial and Ethnic Disparities in COVID-19 Hospitalizations Among US Veterans](#) (28 July 2022)

"In this cohort study, exposure to environmental toxins partially mediated the association of racial and ethnic disparities with COVID-19 hospitalizations, independently of COVID-19–related comorbidities. Exposure to environmental toxins may weaken the respiratory and immune systems of exposed individuals, who disproportionately belong to racial and ethnic minority populations, increasing their susceptibility to serious COVID-19 independently of comorbidities and tobacco use."

### *Return to Duty*

BMJ Mil Health: [Return to flying duties of German military pilots after recovery from COVID-19](#) (22 July 2022)

"Background: Pilots are working in a unique and exacting environment with hypobaric hypoxia and acceleration forces. In military flying, missions are often challenging with possible combat scenarios and in remote areas with impaired infrastructure.

Methods: We analysed all German military pilots and pilot candidates with confirmed SARS-CoV-2 infection, who have all been evaluated prior to their return to flying duties between April 2020 and January 2022 by the German Air Force Centre of Aerospace Medicine. Symptoms, comorbidities, scope of investigations, examination results, vaccination status and aeromedical disposition are described.

Results: 90 pilots (82 active pilots and 8 pilot candidates) with a median age of 35 years (IQR 15 years) were included. 78 pilots (87%) reported symptoms, with median duration of 6 days. Symptoms included influenza-like symptoms (70.0%), headache (45.6%), impaired physical fitness (37.8%), anosmia/ageusia (36.7%), fever (27.8%), exertional dyspnoea (8.9%), memory and concentration disorders (4.4%), diarrhoea (3.3%) and dyspnoea at rest (2.2%). Only one pilot (1.1%) was hospitalised, two (2.2%) required outpatient treatment. All pilots were allowed to return to unrestricted flying duties after the assessment, with eight (8.9%) reporting ongoing mild symptoms.

Conclusion: Due to their demanding working environment, pilots, and other high-hazard employees, should undergo medical evaluation prior to return to their duties to exclude

ongoing symptoms and the development of post-acute COVID-19 or post-COVID-19 syndrome. The scope of examinations may depend on the severity of the disease, comorbidities, the vaccination status, the predominant SARS-CoV-2 variant and the type of aircraft flown."

Aerosp Med Hum Perform: [Return to Flying Duties Following a COVID-19 Booster Dose](#) (01 July 2022)

"INTRODUCTION: Israel began vaccinating with the booster dose of the Pfizer-BioNTech vaccine in July 2021, before the Food and Drug Administration (FDA) authorized the vaccine in September 2021. The first and second vaccines were shown to have several side effects that could possibly affect aircrews' fitness to fly. Thus, the Israel Air Force (IAF) decided on a disqualification period of 24 h following the first vaccine, and 48 h following the second vaccine. The aim of this study was to determine the disqualification period following the booster dose of the vaccine.

METHODS: A survey was conducted among IAF aviators in the Aeromedical Center (AMC) in order to characterize the side effects and their duration following a Pfizer-BioNTech COVID-19 vaccine booster dose.

RESULTS: The most common local side effect was injection site pain. The most common systemic side effects were general weakness, fatigue, and myalgia. Duration of side effects was up to 48 h from vaccine administration among the majority of aircrew members.

CONCLUSION: The IAF AMC policy for the Pfizer-BioNTech COVID-19 vaccine booster dose recipients is to disqualify from flight for 48 h following the vaccination."

## **Long COVID and Other Post-Infectious Findings**

### ***News in Brief***

"Millions of Americans have long COVID. Many of them are no longer working" ([NPR](#)).

"Doctors with disabilities push for change as long COVID affects their workforce" ([Time](#)).

"Heart disease after COVID: what the data say" ([Nature](#)).

### ***Long Reads***

"Encouraged by right-wing doctor groups, desperate patients turn to ivermectin for long Covid" ([STAT](#)).

### ***Special Reports and Other Resources***

HHS: [National Research Action Plan on Long COVID \[pdf\]](#) (August 2022)

"[This report] created in coordination with 14 government departments and agencies, introduces the first U.S. government-wide national research agenda focused on advancing prevention, diagnosis, treatment, and provision of services and supports for individuals and families experiencing Long COVID.

The Research Plan stresses four guiding principles to govern federal government data analysis work: health equity, accelerating and expanding current research, orienting the research effort to improve patient care, and partner engagement. The plan demonstrates innovation in early achievements and highlights the importance of collaboration between the public and private sectors to advance prevention, diagnosis, treatment, and provision of health care, public health, and human services for individuals experiencing Long COVID."

HHS: [Services and Supports for Longer-Term Impacts of COVID-19 \[pdf\]](#) (August 2022)

"[This report] outlines federal services available to the American public to address longer-term effects of COVID-19, including Long COVID and related conditions, as well as other impacts on individuals and families. It provides valuable information in three key areas:

1. Federal supports and services available for people experiencing Long COVID – from how to navigate your rights to how to navigate health care coverage, community services, financial assistance, nutrition and educational questions and more.
2. Resources for health care personnel treating patients with Long COVID, as well as support for health care personnel experiencing stress and trauma related to COVID-19.
3. Services for individuals confronting challenges related to mental health, substance use, and bereavement."

### ***Journal Articles***

Lancet: [Persistence of somatic symptoms after COVID-19 in the Netherlands: an observational cohort study](#) (06 August 2022)

"Background: Patients often report various symptoms after recovery from acute COVID-19. Previous studies on post-COVID-19 condition have not corrected for the prevalence and severity of these common symptoms before COVID-19 and in populations without SARS-CoV-2 infection. We aimed to analyse the nature, prevalence, and severity of long-term symptoms related to COVID-19, while correcting for symptoms present before SARS-CoV-2 infection and controlling for the symptom dynamics in the population without infection.

**Methods:** This study is based on data collected within Lifelines, a multidisciplinary, prospective, population-based, observational cohort study examining the health and health-related behaviours of people living in the north of the Netherlands. All Lifelines participants aged 18 years or older received invitations to digital COVID-19 questionnaires. Longitudinal dynamics of 23 somatic symptoms surrounding COVID-19 diagnoses (due to SARS-CoV-2 alpha [B.1.1.7] variant or previous variants) were assessed using 24 repeated measurements between March 31, 2020, and Aug 2, 2021. Participants with COVID-19 (a positive SARS-CoV-2 test or a physician's diagnosis of COVID-19) were matched by age, sex, and time to COVID-19-negative controls. We recorded symptom severity before and after COVID-19 in participants with COVID-19 and compared that with matched controls.

**Findings:** 76 422 participants (mean age 53.7 years [SD 12.9], 46 329 [60.8%] were female) completed a total of 883 973 questionnaires. Of these, 4231 (5.5%) participants had COVID-19 and were matched to 8462 controls. Persistent symptoms in COVID-19-positive participants at 90–150 days after COVID-19 compared with before COVID-19 and compared with matched controls included chest pain, difficulties with breathing, pain when breathing, painful muscles, ageusia or anosmia, tingling extremities, lump in throat, feeling hot and cold alternately, heavy arms or legs, and general tiredness. In 12.7% of patients, these symptoms could be attributed to COVID-19, as 381 (21.4%) of 1782 COVID-19-positive participants versus 361 (8.7%) of 4130 COVID-19-negative controls had at least one of these core symptoms substantially increased to at least moderate severity at 90–150 days after COVID-19 diagnosis or matched timepoint.

**Interpretation:** To our knowledge, this is the first study to report the nature and prevalence of post-COVID-19 condition, while correcting for individual symptoms present before COVID-19 and the symptom dynamics in the population without SARS-CoV-2 infection during the pandemic. Further research that distinguishes potential mechanisms driving post-COVID-19-related symptomatology is required."

JAMA Otolaryngol Head Neck Surg: [Two-Year Prevalence and Recovery Rate of Altered Sense of Smell or Taste in Patients With Mildly Symptomatic COVID-19](#) (04 August 2022)

"In this cohort study, 88.2% of patients reporting a COVID-19–related smell or taste dysfunction completely recovered within 2 years. A late recovery was observed in 10.9% of patients."

BMC Neurol: [Neurocognitive screening in patients following SARS-CoV-2 infection: tools for triage](#) (30 July 2022)

"Background: Cognitive complaints are common in patients recovering from Coronavirus Disease 2019 (COVID-19), yet their etiology is often unclear. We assess factors that contribute to cognitive impairment in ambulatory versus hospitalized patients during the sub-acute stage of recovery.

**Methods:** In this cross-sectional study, participants were prospectively recruited from a hospital-wide registry. All patients tested positive for SARS-CoV-2 infection using a real-time reverse transcriptase polymerase-chain-reaction assay. Patients  $\leq 18$  years-of-age and those with a pre-existing major neurocognitive disorder were excluded. Participants completed an extensive neuropsychological questionnaire and a computerized cognitive screen via remote telemedicine platform. Rates of subjective and objective neuropsychological impairment were compared between the ambulatory and hospitalized groups. Factors associated with impairment were explored separately within each group.

**Results:** A total of 102 patients (76 ambulatory, 26 hospitalized) completed the symptom inventory and neurocognitive tests  $24 \pm 22$  days following laboratory confirmation of SARS-CoV-2 infection. Hospitalized and ambulatory patients self-reported high rates of cognitive impairment (27-40%), without differences between the groups. However, hospitalized patients showed higher rates of objective impairment in visual memory (30% vs. 4%;  $p = 0.001$ ) and psychomotor speed (41% vs. 15%;  $p = 0.008$ ). Objective cognitive test performance was associated with anxiety, depression, fatigue, and pain in the ambulatory but not the hospitalized group.

**Conclusions:** Focal cognitive deficits are more common in hospitalized than ambulatory patients. Cognitive performance is associated with neuropsychiatric symptoms in ambulatory but not hospitalized patients. Objective neurocognitive measures can provide essential information to inform neurologic triage and should be included as endpoints in clinical trials."

Patient: [Opportunities to Improve Long COVID Care: Implications from Semi-structured Interviews with Black Patients](#) (30 July 2022)

"Background: Long coronavirus disease (COVID) is an emerging condition that could considerably burden healthcare systems. Prior qualitative studies characterize the experience of having long COVID, which is valuable for informing care strategies. However, evidence comes from predominantly White samples. This is a concern because underrepresentation of Black patients in research and intervention development contribute to racial inequities.

**Objective:** To facilitate racial equity in long COVID care, the purpose of this qualitative study was to inform the development of care strategies that are responsive to the experiences and perspectives of Black patients with long COVID in the United States of America.

**Methods:** Using convenience sampling, we conducted race-concordant, semi-structured, and open-ended interviews with Black adults (80% female, mean age = 39) who had long COVID. We transcribed and anonymized the recorded interviews. We analyzed the transcripts using inductive, thematic analysis. Theme development focused on who can help

or hinder strategies for reducing health inequities, what should be done to change care policies or treatment strategies, and when are the critical timepoints for intervention.

Results: We developed four main themes. Participants reported challenges before and after COVID testing. Many participants contacted primary care physicians as a first step for long COVID treatment. However, not all respondents had positive experiences and at times felt dismissed. Without a qualifying diagnosis, participants could not obtain disability benefits, which negatively influenced their employment and increased financial hardship.

Conclusions: There are possible targets for improving long COVID care, from COVID testing through to long-term treatment plans. There is a need to increase long COVID awareness among physicians. Diagnosis and a standardized treatment plan could help patients avoid unnecessary healthcare utilization and obtain comprehensive support."

JAMA Netw Open: [Rates and Factors Associated With Documentation of Diagnostic Codes for Long COVID in the National Veterans Affairs Health Care System](#) (29 July 2022)

"Question: What are the rates, clinical settings, and factors associated with documentation of care related to COVID-19 at 3 or more months after acute infection?

Findings: In this cohort study of 198 601 persons with a positive SARS-CoV-2 test, COVID-19 care was documented in 13.5% of individuals 3 or more months after infection during a mean follow-up of 13.5 months and was documented more commonly in older persons, those with higher comorbidity burden, those with more severe acute COVID-19 presentation, and those who were unvaccinated at the time of infection.

Meaning: These findings provide guidance for health care systems to develop systematic approaches to the evaluation and management of patients who may be experiencing long COVID."

Open Forum Infect Dis: [Cognitive Impairment 13 Months After Hospitalization for COVID-19](#) (26 July 2022)

"This study assessed cognitive function 13 months after hospital discharge for coronavirus disease 2019 (COVID-19), using computer-based cognitive tests. Compared to population norms, 14%–25% of patients were impaired in each dimension, and 53% had cognitive impairment in 1 or more of 4 tests. There was some association with acute COVID-19 disease severity."

Nat Med: [Symptoms and risk factors for long COVID in non-hospitalized adults](#) (25 July 2022)

"Severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2) infection is associated with a range of persistent symptoms impacting everyday functioning, known as post-COVID-19 condition or long COVID. We undertook a retrospective matched cohort study using a UK-based primary care database, Clinical Practice Research Datalink Aurum, to determine

symptoms that are associated with confirmed SARS-CoV-2 infection beyond 12 weeks in non-hospitalized adults and the risk factors associated with developing persistent symptoms. We selected 486,149 adults with confirmed SARS-CoV-2 infection and 1,944,580 propensity score-matched adults with no recorded evidence of SARS-CoV-2 infection. Outcomes included 115 individual symptoms, as well as long COVID, defined as a composite outcome of 33 symptoms by the World Health Organization clinical case definition. Cox proportional hazards models were used to estimate adjusted hazard ratios (aHRs) for the outcomes. A total of 62 symptoms were significantly associated with SARS-CoV-2 infection after 12 weeks. The largest aHRs were for anosmia (aHR 6.49, 95% CI 5.02-8.39), hair loss (3.99, 3.63-4.39), sneezing (2.77, 1.40-5.50), ejaculation difficulty (2.63, 1.61-4.28) and reduced libido (2.36, 1.61-3.47). Among the cohort of patients infected with SARS-CoV-2, risk factors for long COVID included female sex, belonging to an ethnic minority, socioeconomic deprivation, smoking, obesity and a wide range of comorbidities. The risk of developing long COVID was also found to be increased along a gradient of decreasing age. SARS-CoV-2 infection is associated with a plethora of symptoms that are associated with a range of sociodemographic and clinical risk factors."

## **Pregnancy and Postpartum Period**

### ***News in Brief***

"Clinical considerations for monkeypox in people who are pregnant or breastfeeding" ([CDC](#)).

### ***Journal Articles***

Am J Infect Control: [Impact of vaccination and the omicron variant on COVID-19 severity in pregnant women](#) (31 July 2022)

"We compared the clinical course of pregnant women with coronavirus disease 2019 (COVID-19) before and after the emergence of the omicron variant and based on vaccination status. We retrospectively reviewed the electronic medical charts of 224 patients and 82 deliveries from November 1, 2020, to March 7, 2022; of these, 42% were diagnosed during the omicron dominance period. Disease severity and morbidity of COVID-19 were significantly decreased during the omicron era. The vaccination rates among the patients were higher after omicron emergence (31.9%) than before (6.9%). Overall, 4.1% and 25% of patients had severe symptoms, and 2.6% and 16.2% required oxygen therapy in the vaccination and non-vaccination groups, respectively. Overall, patients had a more favorable clinical course in the omicron era; moreover, vaccinated patients were better



protected than non-vaccinated patients, indicating the importance of vaccination against COVID-19."

Ann Intern Med: [Telehealth Strategies for the Delivery of Maternal Health Care : A Rapid Review](#) (26 July 2022)

"Background: Telehealth strategies to supplement or replace in-person maternity care may affect maternal health outcomes.

Purpose: To conduct a rapid review of the effectiveness and harms of telehealth strategies for maternal health care given the recent expansion of telehealth arising from the COVID-19 pandemic, and to produce an evidence map.

Data sources: Systematic searches of MEDLINE, the Cochrane Library, CINAHL, Embase, and Scopus for English-language studies (January 2015 to April 2022).

Study selection: Randomized controlled trials (RCTs) and observational studies of maternal care telehealth strategies versus usual care.

Data extraction: Dual data extraction and risk-of-bias assessment of studies, with disagreements resolved through consensus.

Data synthesis: 28 RCTs and 14 observational studies (n = 44 894) were included. Maternal telehealth interventions supplemented in-person care for most studies of mental health and diabetes during pregnancy, primarily resulting in similar, and sometimes better, clinical and patient-reported outcomes versus usual care. Supplementing in-person mental health care with phone- or web-based platforms or mobile applications resulted in similar or better mental health outcomes versus in-person care. A reduced-visit prenatal care schedule using telehealth to replace in-person general maternity care for low-risk pregnancies resulted in similar clinical outcomes and higher patient satisfaction versus usual care. Overall, telehealth strategies were heterogeneous and resulted in similar obstetric and patient satisfaction outcomes. Few studies addressed disparities, health equity, or harms.

Limitations: Interventions varied, and evidence was inadequate for some clinical outcomes.

Conclusion: Replacing or supplementing in-person maternal care with telehealth generally results in similar, and sometimes better, clinical outcomes and patient satisfaction compared with in-person care. The effect on access to care, health equity, and harms is unclear."

## **Pediatric Population**

### ***News in Brief***

#### *Beyond COVID*

"New studies offer theory on cause of unusual hepatitis cases in kids" ([STAT](#)).

"Pandemic drives largest drop in childhood vaccinations in 30 years — Last year alone, 25 million children missed out on immunizations against infections such as measles and polio, leading to avoidable outbreaks of disease" ([Nature](#)).

#### *Monkeypox*

"First cases of monkeypox in children in U.S. confirmed" ([WP](#)).

"Clinical considerations for monkeypox in children and adolescents" ([CDC](#)).

### ***Journal Articles***

Clin Infect Dis: [BNT162b2 mRNA Vaccination Against COVID-19 is Associated with Decreased Likelihood of Multisystem Inflammatory Syndrome in U.S. Children Ages 5-18 Years](#) (04 August 2022)

"Background: Multisystem inflammatory syndrome in children (MIS-C), linked to antecedent severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection, is associated with considerable morbidity. Prevention of SARS-CoV-2 infection or coronavirus disease 2019 (COVID-19) by vaccination might also decrease MIS-C likelihood.

Methods: In a multicenter case-control public health investigation of children ages 5-18 years hospitalized from July 1, 2021 to April 7, 2022, we compared the odds of being fully vaccinated (two doses of BNT162b2 vaccine  $\geq 28$  days before hospital admission) between MIS-C case-patients and hospital-based controls who tested negative for SARS-CoV-2. These associations were examined by age group, timing of vaccination, and periods of Delta and Omicron variant predominance using multivariable logistic regression.

Results: We compared 304 MIS-C case-patients (280 [92%] unvaccinated) with 502 controls (346 [69%] unvaccinated). MIS-C was associated with decreased likelihood of vaccination (aOR, 0.16 95% CI, 0.10-0.26), including among children ages 5-11 years (aOR, 0.22 95% CI, 0.10-0.52), ages 12-18 years (aOR, 0.10 95% CI, 0.05-0.19), and during the Delta (aOR, 0.06 95% CI, 0.02-0.15) and Omicron (aOR, 0.22 95% CI, 0.11-0.42) variant-predominant periods. This association persisted beyond 120 days after the second dose (aOR, 0.08, 95% CI, 0.03-0.22) in 12-18 year-olds. Among all MIS-C case-patients, 187 (62%) required intensive care unit admission and 280 (92%) vaccine-eligible patients were unvaccinated.

Conclusions: Vaccination with two doses of BNT162b2 is associated with reduced likelihood of MIS-C in children ages 5-18 years. Most vaccine eligible hospitalized patients with MIS-C were unvaccinated."

JAMA Netw Open: [Effectiveness Associated With BNT162b2 Vaccine Against Emergency Department and Urgent Care Encounters for Delta and Omicron SARS-CoV-2 Infection Among Adolescents Aged 12 to 17 Years](#) (03 August 2022)

"Question: What is the durability associated with 2 doses of the BNT162b2 COVID-19 vaccine against Delta- and Omicron-related emergency department and urgent care encounters among adolescents aged 12 to 17 years, and is a third dose associated with improved protection?

Findings: In this case-control study including 3168 adolescents, estimated effectiveness of 2 doses of BNT162b2 was highest against both Delta (89%) and Omicron (73%) less than 2 months after vaccination but waned to 49% against Delta and 16% against Omicron at 6 months and beyond. Estimated effectiveness of 3 doses of BNT162b2 against Omicron was 87%.

Meaning: These findings suggest that third doses are needed to achieve peak protection for adolescents and may help mitigate against a future surge in cases."

JAMA Netw Open: [COVID-19 Vaccination Intentions, Concerns, and Facilitators Among US Parents of Children Ages 6 Months Through 4 Years](#) (03 August 2022)

"Question: What are parents' intentions, concerns, and facilitators to COVID-19 vaccination for their children aged 6 months through 4 years?

Findings: In this cross-sectional study of 2031 US adults with children aged 6 months through 4 years, half indicated they intended to get their child a COVID-19 vaccine at some point, but only one-fifth intended to do so within 3 months of the child's eligibility. The top concerns about and facilitators to COVID-19 vaccination for this age group related to COVID-19 vaccination safety and efficacy.

Meaning: These findings suggest that considerable efforts to increase parental COVID-19 vaccine confidence for children aged 6 months through 4 years may be needed to maximize COVID-19 vaccination for this age group."

Clin Infect Dis: [Longitudinal Immune Response to 3 Doses of Messenger RNA Vaccine Against Coronavirus Disease \(COVID-19\) in Pediatric Patients Receiving Chemotherapy for Cancer](#) (28 July 2022)

"Our study in 21 pediatric cancer patients demonstrates that 3 doses of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) messenger RNA vaccine (BioNTech/Pfizer) elicited both humoral and cellular immunity in most patients during chemotherapy.

Immunity was stronger in children with solid tumors and during maintenance therapy compared to those with hematological malignancies or during intensive chemotherapy."

Pediatrics: [Risk of Myopericarditis After COVID-19 Vaccination in Danish Children Aged 5 to 11 Years](#) (26 July 2022)

"In this prospective Danish cohort study, we found a low risk of myopericarditis following COVID-19 vaccination in children aged 5 to 11 years, as also reported by the Vaccine Adverse Event Reporting System. The phenotype of the single case in this study was mild. We found the risk of myopericarditis relative to the background risk to be similar between children and adolescents. Accordingly, the lower risk of myopericarditis following Pfizer-BioNTech vaccination in children aged 5 to 11 years, compared with immunized adolescents, may reflect an overall lower susceptibility of developing myopericarditis in this age group."

### *Long COVID*

MMWR: [Post-COVID-19 Symptoms and Conditions Among Children and Adolescents — United States, March 1, 2020–January 31, 2022](#) (05 August 2022)

"What is already known about this topic? Children and adolescents might be at risk for certain post-COVID symptoms and conditions.

What is added by this report? Compared with patients aged 0–17 years without previous COVID-19, those with previous COVID-19 had higher rates of acute pulmonary embolism (adjusted hazard ratio = 2.01), myocarditis and cardiomyopathy (1.99), venous thromboembolic event (1.87), acute and unspecified renal failure (1.32), and type 1 diabetes (1.23), all of which were rare or uncommon in this study population.

What are the implications for public health practice? COVID-19 prevention strategies, including vaccination for all eligible persons aged ≥6 months, are critical to preventing SARS-CoV-2 infection and subsequent illness, and reducing the public health impact of post-COVID symptoms and conditions among persons aged 0–17 years."

Arch Clin Neuropsychol: [Neurocognitive and Psychosocial Characteristics of Pediatric Patients With Post-Acute/Long-COVID: A Retrospective Clinical Case Series](#) (29 July 2022)

"Objective: Studies suggest a large number of patients have persistent symptoms following COVID-19 infection—a condition termed "long COVID." Although children and parents often report cognitive difficulties after COVID, very few if any studies have been published including neuropsychological testing.

**Methods:** A retrospective chart review was completed for the first 18 patients referred for a neuropsychological evaluation from a multidisciplinary pediatric post-COVID clinic. The neuropsychological screening battery assessed verbal fluency and category switching, attention, working memory, processing speed, and verbal learning and memory. Patients' caregivers also completed standardized questionnaires regarding day-to-day mood and behavior.

**Results:** At intake, the most common neurologic symptoms reported by caregivers were attention problems (83.3%), fatigue/lethargy (77.7%), sleep disturbance (77.7%), dizziness/vertigo (72.2%), and headaches (72.2%). On rating scales, most caregivers endorsed concerns for depressed mood and anxiety (14/15 and 12/15). A large proportion of patients had difficulties with attention (9/18) and depressed mood/anxiety (13/18) before COVID. On cognitive testing, the majority of the patients performed within or above broad average range ( $\geq 16$ th percentile) across most domains. However, a little over half of the patients performed below average on auditory attention measures.

**Conclusions:** Within our clinically referred sample, children who reported lingering cognitive symptoms after COVID-19 often had a preexisting history of attention and/or mood and anxiety concerns. Many of these patients performed below average in attention testing, but it remains to be seen whether this was due to direct effects of COVID, physical symptoms, and/or preexisting difficulties with attention or mood/anxiety."

JAMA Netw Open: [Post-COVID-19 Conditions Among Children 90 Days After SARS-CoV-2 Infection](#) (22 July 2022)

"Question: What proportion of children infected with SARS-CoV-2 who were tested in emergency departments (EDs) reported post-COVID-19 conditions (PCCs) 90 days after their ED visits?

**Findings:** In this cohort study of 1884 SARS-CoV-2-positive children with 90-day follow-up, 5.8% of patients, including 9.8% of hospitalized children and 4.6% of discharged children, reported PCCs. Characteristics associated with PCCs included being hospitalized 48 hours or more, having 4 or more symptoms reported at the index ED visit, and being 14 years of age or older.

**Meaning:** This study suggests that, given the prevalence of PCCs, appropriate guidance and follow-up are required for children testing positive for SARS-CoV-2."

### *Beyond COVID*

MMWR: [Notes from the Field: Increase in Pediatric Intracranial Infections During the COVID-19 Pandemic — Eight Pediatric Hospitals, United States, March 2020–March 2022](#) (05 August 2022)

"During the first 2 years of the U.S. COVID-19 pandemic, pediatric centers anecdotally reported increased rates of intracranial bacterial infections, many of which were diagnosed during or immediately after an infection with SARS-CoV-2, the virus that causes COVID-19....

During the early COVID-19 pandemic, isolated intracranial abscess increased in the participating institutions by a mean of 100.9% (SD = 133%), and sinusitis complicated by intracranial abscess increased by a mean of 76.7% (SD = 97%). Orbital cellulitis, sinusitis, and mastoiditis all decreased on average by 14.5% (SD = 31%), 31.9% (SD = 17%), and 24.7% (SD = 31%), respectively (Figure). Mastoiditis complicated by intracranial abscess decreased by 116.7% (SD = 96%)....

On June 8, 2022, CDC asked health care providers and health departments to report the occurrence of brain abscess, epidural empyema, or subdural empyema in persons aged ≤18 years without a previous history of neurosurgical procedures or head trauma, hospitalized on or after June 1, 2021, and to retain associated clinical specimens and isolates. To report possible cases, health care providers should contact their health department and email CDC (CDCStrepInquiry@cdc.gov).

This initial investigation suggests a possible increase in some forms of intracranial infections in persons aged ≤18 years living in the United States during March 2020–March 2022, coinciding with the first 2 years of the COVID-19 pandemic."

J Sch Health: [Military Adolescent Pandemic Study 2021: MAPS21](#) (02 August 2022)

"Background: Military-connected students move between 6 to 9 times throughout their K-12 experience, creating unique challenges relating to integration, adaptation, identity development, and acceptance. However, when transitions occur during a global pandemic, isolation and disconnect with schools and the community create new challenges that impact health and well-being. The MAPS21 study uncovers the lived experiences of military-connected students who have experienced a transition during the pandemic and gives rise to the need for interdisciplinary care within the public-school setting to promote mental health and academic support during and post-pandemic transitions.

Methods: Military adolescents and their parent(s) were interviewed and data were analyzed following an interpretive phenomenological process. A social-ecological model served as the guide to understand the participants' experiences and to further inform future supportive measures.

Results: Seven subthemes surface under Individual, Relationships, Community, and Society and Policy, the levels within the social-ecological model. These subthemes included: anticipatory processes, control, growth and maturity, adapting views, isolation, school support, community support.

Conclusion: Military-connected students may experience adverse outcomes relating to mental health and academic progression after experiencing a move during the pandemic. This study provides an avenue for teams of interdisciplinary professionals to collaborate within the public-school setting to provide proactive support through engagement and policy development."

## **Other Infectious Diseases and Public Health Threats**

### ***News in Brief***

The NY polio case is tied to viruses detected in U.K. and Israel ([STAT](#)) and polioviruses have been detected in wastewater samples ([STAT](#)).

"Typhoid mutated to beat antibiotics. Science is learning how to beat those strains" ([NPR](#)).

"One dead, 11 sickened by Legionnaires' disease in California's Napa County" ([NBC](#)).

### ***Journal Articles***

J Infect Dis: [Prolonged shedding of Zika virus in human semen is associated with male reproductive tract inflammation](#) (04 August 2022)

"Zika virus (ZIKV) is a mosquito-borne flavivirus that causes congenital defects. Sexual transmission of ZIKV was confirmed in a recent epidemic; however, mechanisms behind ZIKV infection and persistence in the male reproductive tract are unknown. Previously, we found that ~33% of men with symptomatic ZIKV infections shed ZIKV RNA in semen, and some men shed ZIKV RNA for >3 months. Here, we evaluated the semen of 49 ZIKV-infected men to identify immune factors correlating with long-term ZIKV shedding in semen and ZIKV-infected cell types in semen. We found prolonged ZIKV RNA shedding in semen was associated with male reproductive tract inflammation, indicated by higher leukocyte counts and inflammatory cytokine concentrations in semen of long-term versus short-term shedders. Additionally, we found ZIKV RNA in seminal leukocytes and epithelial cells. This study of human semen from ZIKV-infected men provides critical insights into impacts of ZIKV on male reproductive tract health." See also: [commentary](#)



## **Special Topic: Monkeypox**

### ***News in Brief***

As of 23 July 2022, the WHO has declared the current monkeypox outbreak a public health emergency ([WHO](#)).

04 August 2022: "U.S. declares monkeypox outbreak a public health emergency" ([STAT](#)).

"US now has more monkeypox cases than any other non-endemic country" ([CIDRAP](#)).

"Red Cross beginning to screen blood donors for monkeypox" ([STAT](#)).

"Monkeypox originated in animals. Could it spill back into them? The zoonotic disease is now spreading from person to person. But if it finds a home in new wildlife species, it could settle in to become a permanent risk" ([Wired](#)).

### ***Vaccines***

"How well does the monkeypox vax work? No one knows for sure" ([Medpage](#)).

"Moderna considering creating an mRNA monkeypox vaccine amid growing demand for shots" ([ABC](#)).

### ***Stigma***

"How we talk about monkeypox matters. Experts offer ways to reduce stigma" ([NPR](#)).

"The campaign to rename monkeypox gets complicated" ([STAT](#)).

### ***Long Reads***

"He discovered the origin of the monkeypox outbreak — and tried to warn the world" ([NPR](#)).

## ***Webinars and Other Events***

TOPIC: The Global Monkeypox Outbreak

"Johns Hopkins University will host a live virtual briefing about the global monkeypox outbreak, which the World Health Organization director-general declared a Public Health Emergency of International Concern in late July. In the U.S., the Biden administration has also declared a public health emergency for monkeypox."

WHEN: Wednesday, 10 August 2022 1030–1130 EDT

REGISTER OR WATCH LIVE STREAM: <https://hub.jhu.edu/monkeypox-briefing/>

WHAT: CDC Clinician Outreach and Communication Activity (COCA)

TOPIC: Monkeypox Outbreak: Updates on the Epidemiology, Testing, Treatment, and Vaccination

"This COCA Call will provide updates on the epidemiology of the monkeypox outbreak, commercial testing capability, how to obtain and use TPOXX (tecovirimat) to treat monkeypox, and vaccine strategy."

WHEN: Recorded Tuesday, 26 July 2022

LINK: [https://emergency.cdc.gov/coca/calls/2022/callinfo\\_072622.asp](https://emergency.cdc.gov/coca/calls/2022/callinfo_072622.asp)

### ***Journal Articles***

Clin Infect Dis: [Antivirals with Activity Against Monkeypox: A Clinically Oriented Review](#) (29 July 2022)

"Monkeypox virus is an emergent human pathogen. While it is less lethal than smallpox, it can still cause significant morbidity and mortality. In this review, we explore three antiviral agents with activity against monkeypox and other orthopoxviruses: cidofovir, brincidofovir, and tecovirimat. Cidofovir, and its prodrug brincidofovir, are inhibitors of DNA replication with a broad spectrum of activity against multiple families of double-stranded DNA viruses. Tecovirimat has more specific activity against orthopoxviruses, and inhibits the formation of the extracellular enveloped virus necessary for cell-to-cell transmission. For each agent, we review basic pharmacology, data from animal models and reported experience in human patients."

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